

CLAIMS

1. A method for the treatment and/or prophylaxis of an osteonecrotic bone disease in a mammal in need thereof, such as, e.g., idiopathic or secondary osteonecrosis, avascular bone necrosis, glucocorticoid induced bone ischemia/osteonecrosis, Legg-Calve-Perthes disease and femoral head necrosis, the method comprising administering an effective dose of a strontium-containing compound (a) to the mammal.
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2. A method according to claim 1, wherein the daily dose of strontium is at least about 0.01 g, such as, e.g. at least about 0.025 g, at least about 0.050 g, at least about 0.075 g, at least about 0.1 g, at least about 0.2 g, at least about 0.3 g, at least about 0.4 g or at least about 0.5 g or from about 0.01 to about 2 g such as, e.g., from about 0.1 to about 2 g, from about 0.1 to about 1 g, from about 0.15 to about 0.5 g, from about 0.3 to about 2 g or from about 0.5 to about 2 g.
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3. A method according to claim 1 or 2, wherein the administration takes place one or more times daily.
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4. A method according to claim 3, wherein the administration takes place from 2-5 times daily.
5. A method according to any of the preceding claims, wherein the administration is by the enteral or parenteral route or by topical administration.
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6. A method according to claim 5, wherein the administration is by the oral route.
7. A method for the treatment and/or prophylaxis of an osteonecrotic bone disease, such as, e.g., idiopathic or secondary osteonecrosis, avascular bone necrosis, glucocorticoid induced bone ischemia/osteonecrosis and femoral head necrosis, in a mammal who is to be or is treated with a therapeutic agent (b) known to or suspected of inducing apoptosis and/or necrosis of bone cells, the method comprising administering a strontium-containing compound (a) in combination with (b).
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8. A method according to claim 7, wherein the apoptosis and/or necrosis of bone cells lead to an osteonecrotic bone disease.
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9. A method according to claim 7 or 8, wherein the administration of the strontium-

containing compound (a) and the therapeutic agent (b) leads to at least one of the following:

- i) reduction in the incidence or severity of the osteonecrotic bone disease, wherein the incidence or severity of the osteonecrotic bone disease is reduced by at least 5%, such as, e.g., at least 10%, at least 20%, at least 30%, at least 40% or at least 50% in patients treated with (a) and (b) in combination as compared to patients treated with (b) alone in the same dose as (b) in the combination treatment,
- ii) reduction of frequency and/or magnitude of side-effects of (b), wherein side effects are being defined as any clinical relevant observation pertaining to the disease or condition in the patient, such as bone-pain, joint-pain, immobility, functional impairment, weight loss or bone mineral density (BMD) decrease, and wherein the frequency and/or magnitude of the side-effects is reduced by at least 5%, such as, e.g., at least 10%, at least 20%, at least 30%, at least 40% or at least 50% in patients treated with (a) and (b) in combination as compared to patients treated with (b) alone in the same dose as (b) in the combination treatment.

10. A method according to any of claims 7-9, wherein the therapeutic agent (b) is a glucocorticoid and/or another steroid hormone.

11. A method according to any of claims 7-9, wherein the therapeutic agent (b) is an anti-retroviral compound, such as, e.g., efavirenz (Sustiva®), zidovudine (Retrovir®), lamivudine (Epivir®), abacavir (Ziagen®), zalcitabine (Hivid®), didanosine (Videx®), stavudine (Zerit®), tenofovir disoproxil fumarate (Viread®), emtricitabine (Emtriva®), fosamprenavir (Lexiva®), nevirapine (Viramune®), delavirdine (Rescriptor®), capravirine, enfuvirtide (Fuzeon®), saquinavir (Invirase®, Fortovase®), ritonavir (Norvir®), indinavir (Crixivan®), tipranavir, amdoxovir, elvucitabine, atazanavir (Reyataz®), nelfinavir (Viracept®), amprenavir (Agenerase®), PRO-542, TMC-114, TMC-125, BMS-56190, DPC-0830, .

12. A method according to any of claims 7-9, wherein the therapeutic agent (b) is a bisphosphonate.

35 13. A method according to any of claims 7-12, wherein the daily dose of strontium is at least about 0.01 g, such as, e.g. at least about 0.025 g, at least about 0.050 g, at least about 0.075 g, at least about 0.1 g, at least about 0.2 g, at least about 0.3 g, at least about

0.4 g or at least about 0.5 g or from about 0.01 to about 2 g such as, e.g., from about 0.1 to about 2 g, from about 0.1 to about 1 g, from about 0.15 to about 0.5 g, from about 0.3 to about 2 g or from about 1 to about 2 g.

- 5 14. A method according to any of claims 7-13, wherein (a) and (b) are administered as a single composition.
- 10 15. A method according to any of claims 7-13, wherein (a) and (b) are administered as separate compositions.
16. A method according to any of claims 7-15, wherein the administration of (a) and (b) take place simultaneously or sequentially.
17. A method according to any of claims 1 to 16, wherein the strontium-containing compound (a) is selected from the group consisting of strontium salts of an organic or an inorganic acid.
18. A method according to claim 17, wherein the salt is in hydrate, anhydrous, solvate, polymorphous, amorphous, crystalline, microcrystalline or polymeric form.
- 20 19. A method according to any of claims 1-18, wherein the salt is selected from the group comprising strontium chloride, strontium carbonate, strontium citrate, strontium malonate, strontium succinate, strontium fumarate, strontium ascorbate, strontium pyruvate, strontium L-glutamate, strontium D-glutamate, strontium L-aspartate, strontium D-aspartate, strontium alpha-ketoglutarate, strontium lactate, strontium tartrate, strontium glutarate, strontium maleate, strontium methanesulfonate, strontium benzenesulfonate, strontium ranelate and mixtures thereof.
- 30 20. Use of a strontium-containing compound (a) for the manufacture of a medicament for treating and/or preventing an osteonecrotic bone condition, such as, e.g. idiopathic or secondary osteonecrosis, avascular bone necrosis, glucocorticoid induced bone ischemia/osteonecrosis, Legg-Calve-Perthes disease and femoral head necrosis, in a mammal.
- 35 21. Use of a strontium containing-compound (a) and a therapeutic agent (b) for the manufacture of a medicament for treating and/or preventing an osteonecrotic bone condition in a mammal, wherein (b) is known to or suspected of inducing apoptosis and/or

necrosis of bone cells leading to an osteonecrotic bone condition.

22. A pharmaceutical composition comprising a strontium-containing compound (a), and a therapeutic agent (b) that is known to or suspected of inducing apoptosis and/or necrosis
5 of bone cells leading to an osteonecrotic bone condition, optionally together with one or more pharmaceutically acceptable excipients.
23. A kit comprising two or more components, the first component comprising a strontium-containing compound (a) and the second component comprising a therapeutic agent (b)
10 that is known to or suspected of inducing apoptosis and/or necrosis of bone cells leading to an osteonecrotic bone condition.